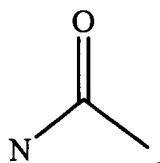


IN THE CLAIMS

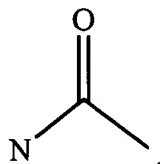
1. (Currently amended) A bisubstrate inhibitor of insulin receptor kinase, comprising:
a nucleotide or nucleotide analog moiety;
and a peptide moiety which is a substrate for said insulin receptor kinase;
wherein said moieties are linked by a tether that comprises a proton donor,
wherein the tether is ≥ 4.9 Å measured from a gamma phosphorus of the
nucleotide or nucleotide analog moiety to the proton donor.
2. (Original) The bisubstrate inhibitor of claim 1 wherein the nucleotide or nucleotide
analog moiety is ATP.
3. (Original) The bisubstrate inhibitor of claim 1 wherein the nucleotide or nucleotide
analog moiety is γ -S-ATP.
4. (Original) The bisubstrate inhibitor of claim 1 wherein the peptide comprises a
tyrosine residue in which its phenolic oxygen is replaced with a nitrogen atom.
5. (Original) The bisubstrate inhibitor of claim 1 wherein the peptide moiety has at least
4 contiguous amino acid residues selected from the sequence Lys, Lys, Lys, Leu,
Pro, Ala, Thr, Gly, Asp, Tyr, Met, Asn, Met, Ser, Pro, Val, Gly, Asp (SEQ ID
NO:1).
6. (Original) The bisubstrate inhibitor of claim 1 wherein the peptide moiety has at least
5 contiguous amino acid residues selected from the sequence Lys, Lys, Lys, Leu,
Pro, Ala, Thr, Gly, Asp, Tyr, Met, Asn, Met, Ser, Pro, Val, Gly, Asp (SEQ ID
NO:1).
7. (Original) The bisubstrate inhibitor of claim 1 wherein the peptide moiety comprises
the sequence Lys, Lys, Lys, Leu, Pro, Ala, Thr, Gly, Asp, Tyr, Met, Asn, Met,
Ser, Pro, Val, Gly, Asp (SEQ ID NO:1).
8. (Original) The bisubstrate inhibitor of claim 1 wherein the nucleotide or nucleotide
analog moiety is a nucleotide in which one or more phosphate groups are replaced
by uncharged alkyl groups.
9. (Original) The bisubstrate inhibitor of claim 1 wherein the nucleotide or nucleotide
analog moiety is a nucleotide in which one or more phosphate groups are replaced
by uncharged C₁ to C₃ alkyl groups.

10. (Original) The bisubstrate inhibitor of claim 1 wherein the peptide moiety comprises a membrane translocating sequence (MTS).
11. (Original) The bisubstrate inhibitor of claim 10 wherein the MTS is at the N-terminus of the peptide moiety.
12. (Original) The bisubstrate inhibitor of claim 10 wherein the MTS is at the C-terminus of the peptide moiety.
13. (Original) The bisubstrate inhibitor of claim 1 wherein the peptide moiety comprises an HIV TAT sequence.
14. (Original) The bisubstrate inhibitor of claim 1 wherein the peptide moiety comprises carbon-carbon bonds in place of amide bonds.
15. (Currently amended) A bisubstrate inhibitor of insulin kinase, comprising:
a nucleotide or nucleotide analog moiety;
and a peptide moiety which is a substrate for said insulin receptor kinase;
wherein said moieties are linked by a tether that comprises a proton donor,
wherein the tether is ≥ 4.9 Å measured from a gamma phosphorus of the
nucleotide or nucleotide analog moiety to the proton donor, wherein the
bisubstrate inhibitor of insulin receptor kinase ~~The bisubstrate inhibitor for the~~
~~insulin receptor tyrosine kinase of claim 1 which is Compound 2.~~
- 16-57. (Canceled)
58. (Original) The bisubstrate inhibitor of claim 1 which is bound to insulin receptor kinase.
59. (Canceled)
60. (Currently amended) A bisubstrate inhibitor of a protein kinase comprising:
a nucleotide or nucleotide analog moiety; and
a peptide moiety which is a substrate for said protein kinase;
wherein said moieties are linked by a tether that comprises a proton donor,
wherein the tether is ≥ 4.9 Å measured from a gamma phosphorus of the
nucleotide or nucleotide analog to the proton donor.
61. (Canceled)
62. (Canceled)

63. (Original) The bisubstrate inhibitor of claim 60 wherein the protein kinase is a tyrosine protein kinase.
64. (Canceled)
65. (Canceled)
66. (Currently amended) The bisubstrate inhibitor of claim 63 wherein a nitrogen atom replaces a hydroxyl oxygen on a ~~the~~ tyrosine.
67. (Original) The bisubstrate inhibitor of claim 60 which is bound to the protein kinase.
68. Canceled)
69. (New) The bisubstrate inhibitor of claim 60 wherein the peptide moiety comprises at least 4 contiguous amino acids of a natural substrate of said protein kinase.
70. (New) The bisubstrate inhibitor of claim 60 wherein the peptide moiety comprises at least 5 contiguous amino acids of a natural substrate of said protein kinase.
71. (New) The bisubstrate inhibitor of claim 60 wherein the peptide moiety comprises at least 6 contiguous amino acids of a natural substrate of said protein kinase.
72. (New) The bisubstrate inhibitor of claim 1 wherein the tether is



73. (New) The bisubstrate inhibitor of claim 60 wherein the tether is



74. (New) The bisubstrate inhibitor of claim 60 wherein the peptide moiety is a natural substrate of said protein kinase.
75. (New) The bisubstrate inhibitor of claim 60 wherein the nucleotide or nucleotide analog moiety is a substrate for said protein kinase.

76. (New) The bisubstrate inhibitor of claim 1 wherein the nucleotide or nucleotide analog moiety is a substrate for said insulin receptor kinase.